2017 ESC Pocket Guidelines

Committee for Practice Guidelines

AMI-STEMI

2017 ESC Guidelines for thh Management of Acute Myocardial Infarction in Patients Presenting with ST-Segment Elevation

ESC
European Society of Cardiology

www.escardio.org/guidelines

Introduction

Overview

Updates on the management of patients presenting with ST-segment elevation myocardial infarction (STEMI) should be based on sound evidence, derived from well-conducted clinical trials whenever possible, or motivated expert opinion when needed. It must be recognized that even when excellent clinical trials have been undertaken, the results are open to interpretation, and treatments may need to be adapted to take account of clinical circumstances and resources.

Definition of acute MI

The term acute myocardial infarction (AMI) should be used when there is evidence of myocardial injury (defined as an elevation of cardiac troponin values with at least one value above the 99th percentile upper reference limit) with necrosis in a clinical setting consistent with myocardial ischaemia. For the sake of immediate treatment strategies such as reperfusion therapy, it is usual practice to designate patients with persistent chest discomfort or other symptoms suggestive of ischaemia and ST-segment elevation in at least two contiguous leads as STEMI.

Epidemiology of STEMI

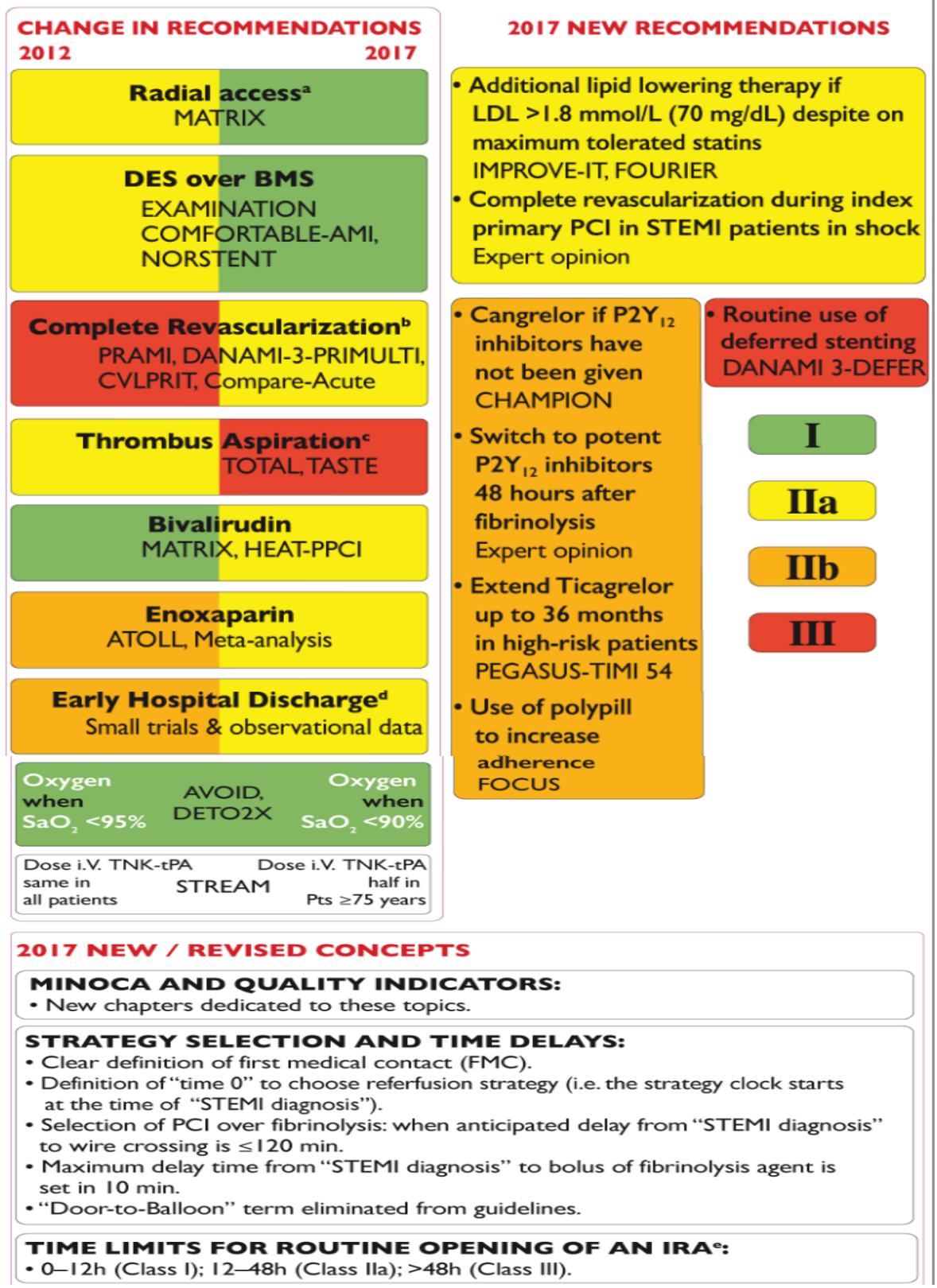
Worldwide, ischaemic heart disease is the single most common cause of death and its frequency is increasing. However, in Europe there has been an overall trend for a reduction in ischaemic heart disease mortality during the past three decades. Ischaemic heart disease now accounts for almost 1.8 million annual deaths, or 20% of all deaths in Europe, although with large variations between countries.

The relative incidences of STEMI are decreasing and NSTEMI are increasing. There is a consistent pattern for STEMI to be relatively more common in younger than in older people, and more common in men than in women.

Several recent studies have highlighted a fall in acute and long-term mortality following STEMI in parallel with greater use of reperfusion therapy, primary percutaneous coronary intervention (PCI), modern antithrombotic therapy, and secondary prevention. Still, mortality remains substantial: the in-hospital mortality of unselected patients with STEMI in the national registries of the ESC countries varies between 4% and 12%, while reported one-year mortality among STEMI patients in angiography registries is approximately 10%.

Although ischaemic heart disease develops on average 7–10 years later in women compared with men, myocardial infarction remains a leading cause of death in women. Acute coronary syndrome (ACS) occurs three to four times more often in men than in women below the age of 60, but after the age of 75, women represent the majority of patients. There is an ongoing debate on whether outcomes are poorer in women, with several studies indicating that a poorer outcome is related to older age and more comorbidities among women suffering myocardial infarction. Some studies have indicated that women tend to undergo fewer interventions than men and receive reperfusion therapy less frequently. These guidelines aim to highlight the fact that women and men receive equal benefit from a reperfusion strategy and STEMI-related therapy, and both genders must be managed in a similar fashion.

Figure 1 What is new in 2017 Guidelines on AMI-STEMI



2017 NEW / REVISED CONCEPTS

MINOCA AND QUALITY INDICATORS:
- New chapters dedicated to these topics.

STRATEGY SELECTION AND TIME DELAYS:
- Clear definition of first medical contact (FMC).
- Definition of "time 0" to choose reperfusion strategy (i.e. the strategy clock starts at the time of "STEMI diagnosis").
- Selection of PCI over fibrinolysis: when anticipated delay from "STEMI diagnosis" to wire crossing is ≤120 min.
- Maximum delay time from "STEMI diagnosis" to bolus of fibrinolysis agent is set in 10 min.
- "Door-to-Balloon" term eliminated from guidelines.

TIME LIMITS FOR ROUTINE OPENING OF AN IRA[e]:
- 0–12h (Class I); 12–48h (Class IIa); >48h (Class III).

ELECTROCARDIOGRAM AT PRESENTATION:
- Left and right bundle branch block considered equal for recommending urgent angiography if ischaemic symptoms.

TIME TO ANGIOGRAPHY AFTER FIBRINOLYSIS:
- Timeframe is set in 2–24h after successful fibrinolysis.

PATIENTS TAKING ANTICOAGULANTS:
- Acute and chronic management presented.

BMS = bare metal stent; DES = drug eluting stent; IRA = infarct related artery; *i.v.* = intravenous; LDL = low-density lipoprotein; PCI = percutaneous coronary intervention; SaO2 = arterial oxygen saturation; STEMI = ST-elevation myocardial infarction; TNK-tPA = Tenecteplase tissue plasminogen activator. For explanation of trial names, see list of abbreviations and acronyms.

[a]Only for experienced radial operators.

[b]Before hospital discharge (either immediate or staged)

[c]Routine thrombus aspiration (bailout in certain cases may be considered).

[d]In 2012 early discharge was considered after 72h, in 2017 early discharge is 48–72h.

[e]If symptoms or haemodynamic instability IRA should be opened regardless time from symptoms onset. In left and mid panels, below each recommendation, the most representative trial (acronym) driving the indication is mentioned.

Management – including diagnosis and treatment – of STEMI starts from the point of first medical contact (FMC). It is recommended to establish a regional reperfusion strategy to maximize efficiency.

A working diagnosis of STEMI (called the "STEMI diagnosis" throughout this document) must first be made. This is usually based on symptoms consistent with myocardial ischaemia (i.e. persistent chest pain) and signs (i.e. 12-lead ECG).

When a STEMI is suspected, a 12-lead ECG must be acquired and interpreted as soon as possible at the time of FMC to facilitate early STEMI diagnosis and triage. In patients with a clinical suspicion of myocardial ischaemia and ST-segment elevation, reperfusion therapy needs to be initiated as soon as possible.

ECG criteria are based on changes of electrical currents of the heart (measured in miliVolts). Standard calibration of the ECG is 10mm/mV. Therefore 0.1 mV equals to 1 mm square on the vertical axis. For simplicity, in this document ECG deviations are expressed in mm following the standard calibration.

In the proper clinical context, ST-segment elevation (measured at the J-point) is considered suggestive of ongoing coronary artery acute occlusion in the following cases: ≥2 contiguous leads with ST-segment elevation ≥2.5 mm in men <40 years, ≥2 mm in men ≥40 years, or ≥1.5 mm in women in leads V_2 –V_3 and/or ≥1 mm in the other leads. In patients with inferior myocardial infarction, it is recommended to record right precordial leads (V_3R and V_4R) seeking ST-segment elevation, to identify concomitant right ventricular (RV) infarction. Likewise, ST-segment depression in leads V_1–V_3 suggests myocardial ischaemia, especially when the terminal T-wave is positive (ST-segment elevation equivalent), and confirmation by concomitant ST-segment elevation ≥0.5 mm recorded in leads V_7 –V_9 should be considered as a means to identify posterior myocardial infarction. The presence of a Q wave on the ECG should not necessarily change the reperfusion strategy decision.

Blood sampling for serum markers is routinely carried out in the acute phase. This is indicated, but should not delay the reperfusion strategy/treatment. If in doubt regarding the possibility of acute evolving myocardial infarction, emergency imaging aids the provision of timely reperfusion therapy to these patients.

Recommendations for initial diagnosis		
Recommendations	**Class[a]**	**Level[b]**
ECG monitoring		
12-lead ECG recording and interpretation is indicated as soon as possible at the point of FMC, with a maximum target delay of 10 min.	I	B
ECG monitoring with defibrillator capacity is indicated as soon as possible in all patients with suspected STEMI.	I	B
The use of additional posterior chest wall leads (V_7–V_9) in patients with high suspicion of posterior myocardial infarction (circumflex occlusion) should be considered.	IIa	B
The use of additional right precordial leads (V_3R and V_4R) in patients with inferior myocardial infarction should be considered to identify concomitant RV infarction.	IIa	B
Blood sampling		
Routine blood sampling for serum markers is indicated as soon as possible in the acute phase but should not delay reperfusion treatment.	I	C

Table 3 Atypical electrocardiographic presentations that should prompt a primary percutaneous coronary intervention strategy in patients with ongoing symptoms consistent with myocardial ischaemia

Bundle branch block

Criteria that can be used to improve the diagnostic accuracy of STEMI in LBBB:

- Concordant ST-segment elevation ≥1 mm in leads with a positive QRS complex
- Concordant ST-segment depression ≥1 mm in V_1–V_3
- Discordant ST-segment elevation ≥5 mm in leads with a negative QRS complex

The presence of RBBB may confound the diagnosis of STEMI.

Ventricular paced rhythm

During RV pacing, the ECG also shows LBBB and the above rules also apply for the diagnosis of myocardial infarction during pacing; however, they are less specific.

Isolated posterior myocardial infarction

Isolated ST depression ≥0.5 mm in leads V_1–V_3 and ST-segment elevation (≥0.5 mm) in posterior chest wall leads V_7–V_9.

Ischaemia due to left main coronary artery occlusion or multivessel disease

ST depression ≥1 mm in eight or more surface leads, coupled with ST-segment elevation in aVR and/or V1, suggests left main-, or left main equivalent- coronary obstruction, or severe three vessel ischaemia.

Relief of hypoxaemia and symptoms		
Recommendations	**Class[a]**	**Level[b]**
Hypoxia		
Oxygen is indicated in patients with hypoxaemia (SaO_2 <90% or PaO_2 <60 mmHg).	I	C
Routine oxygen is not recommended in patients with SaO_2 ≥90%.	III	B
Symptoms		
Titrated *i.v.* opioids should be considered to relieve pain.	IIa	C
A mild tranquillizer (usually a benzodiazepine) should be considered in very anxious patients.	IIa	C

i.v. = intravenous; PaO2 = partial pressure of oxygen; SaO2 = arterial oxygen saturation.

Many deaths occur very early after STEMI onset, due to ventricular fibrillation (VF). As this arrhythmia frequently occurs at an early stage, these deaths usually happen out of hospital.

In patients following cardiac arrest and ST-segment elevation on the ECG, primary PCI is the strategy of choice. Given the high prevalence of coronary occlusions and potential difficulties in interpreting the ECG in patients after cardiac arrest, urgent angiography (within 2 hours) should be considered in survivors of cardiac arrest, including unresponsive survivors, having a high index of suspicion of ongoing infarction (such as the presence of chest pain before arrest, history of established CAD, and abnormal or uncertain ECG results). However, in patients without ST-segment elevation, a quick evaluation at the emergency department or intensive cardiac care unit to exclude non-coronary causes and to perform an urgent echocardiography is reasonable. Unfavourable pre-hospital settings indicating a remote likelihood for neurological recovery should be strongly considered and argued against an invasive coronary strategy.

Prevention and improved treatment of out-of-hospital cardiac arrest is crucial for reducing the mortality related to CAD.

Cardiac arrest		
Recommendations	**Class[a]**	**Level[b]**
A primary PCI strategy is recommended in patients with resuscitated cardiac arrest and an ECG consistent with STEMI.	I	B
Targeted temperature management[c] is indicated early after resuscitation of cardiac arrest patients who remain unresponsive.	I	B
It is indicated that healthcare systems implement strategies to facilitate transfer of all patients in whom a myocardial infarction is suspected directly to the hospital offering 24/7 PCI-mediated reperfusion therapy via one specialized EMS.	I	C
It is indicated that all medical and paramedical personnel caring for suspected myocardial infarction have access to defibrillation equipment and are trained in basic cardiac life support.	I	C
Urgent angiography (and PCI if indicated) should be considered in patients with resuscitated cardiac arrest without diagnostic ST- segment elevation but with a high suspicion of ongoing myocardial ischaemia.	IIa	C
Pre-hospital cooling using a rapid infusion of large volumes of cold *i.v.* fluid immediately after return of spontaneous circulation is not recommended.	III	B

24/7 = 24 hours a day, 7 days a week; ECG = electrocardiogram; EMS = emergency medical system; *i.v.* = intravenous; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

[a]Class of recommendation.

[b]Level of evidence.

[c]Targeted temperature management refers to active methods (i.e. cooling catheters, cooling blankets, and application of ice applied around the body) to achieve and maintain a constant specific body temperature between 32°C and 36°C in a person for a specific duration of time (most commonly used ≥24 hours).

To minimize patient delay, it is recommended to increase public awareness of how to recognize common symptoms of AMI and to call the emergency services. All components of the system delay represent the quality of care and it is recommended to measure them as quality indicators.

System delay is more readily modifiable by organizational measures than is patient delay, and it is a predictor of outcomes. When STEMI diagnosis is made in the pre-hospital setting (EMS), activation of the catheterization laboratory not only reduces treatment delays but may also reduce patient mortality.

Optimal treatment of STEMI should be based on implementation of networks between hospitals. The goal of these networks is to provide optimal care while minimizing delays, thereby improving clinical outcomes. Cardiologists should actively collaborate with all stakeholders, particularly emergency physicians, in establishing such networks.

The main features of such a network are:

- Clear definition of geographic areas of responsibility.
- Shared written protocols.
- Pre-hospital triage of STEMI patients to the appropriate institution, bypassing non-PCI hospitals or hospitals without a 24/7 primary PCI programme.
- On arrival at the appropriate hospital, the patient should immediately be taken to the catheterization laboratory, bypassing the emergency department.
- Patients presenting to a non–PCI-capable hospital and awaiting transportation for primary or rescue PCI must be attended in an appropriate monitored and staffed area.
- If the diagnosis of STEMI has not been made by the ambulance crew, and the ambulance arrives at a non–PCI-capable hospital, the ambulance should await the diagnosis and, if a STEMI diagnosis is made, should continue to a PCI-capable hospital.

Logistics of pre-hospital care		
Recommendations	**Class[a]**	**Level[b]**
It is recommended that the pre-hospital management of STEMI patients is based on regional networks designed to deliver reperfusion therapy expeditiously and effectively, with efforts made to make primary PCI available to as many patients as possible.	I	B
It is recommended that primary PCI-capable centres deliver a 24/7 service and are able to perform primary PCI without delay.	I	B
It is recommended that patients transferred to a PCI-capable centre for primary PCI bypass the emergency department and CCU/ICCU and are transferred directly to the catheterization laboratory.	I	B
It is recommended that ambulance teams are trained and equipped to identify STEMI (with use of ECG recorders and telemetry as necessary) and administer initial therapy, including fibrinolysis when applicable.	I	C
It is recommended that all hospitals and EMS participating in the care of patients with STEMI record and audit delay times and work to achieve and maintain quality targets.	I	C
It is recommended that EMS transfer STEMI patients to a PCI-capable centre, by-passing non-PCI centres.	I	C
It is recommended that EMS, emergency departments, and CCU/ ICCU have a written updated STEMI management protocol, preferably shared within geographic networks.	I	C
It is recommended that patients presenting to a non-PCI-capable hospital and awaiting transportation for primary or rescue PCI are attended in an appropriately monitored area (e.g. the emergency department, CCU/ICCU, intermediate care unit).	I	C

24/7 = 24 hours a day, 7 days a week; CCU = coronary care unit; ECG = electrocardiogram; EMS = emergency medical system; ICCU = intensive cardiac care unit; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

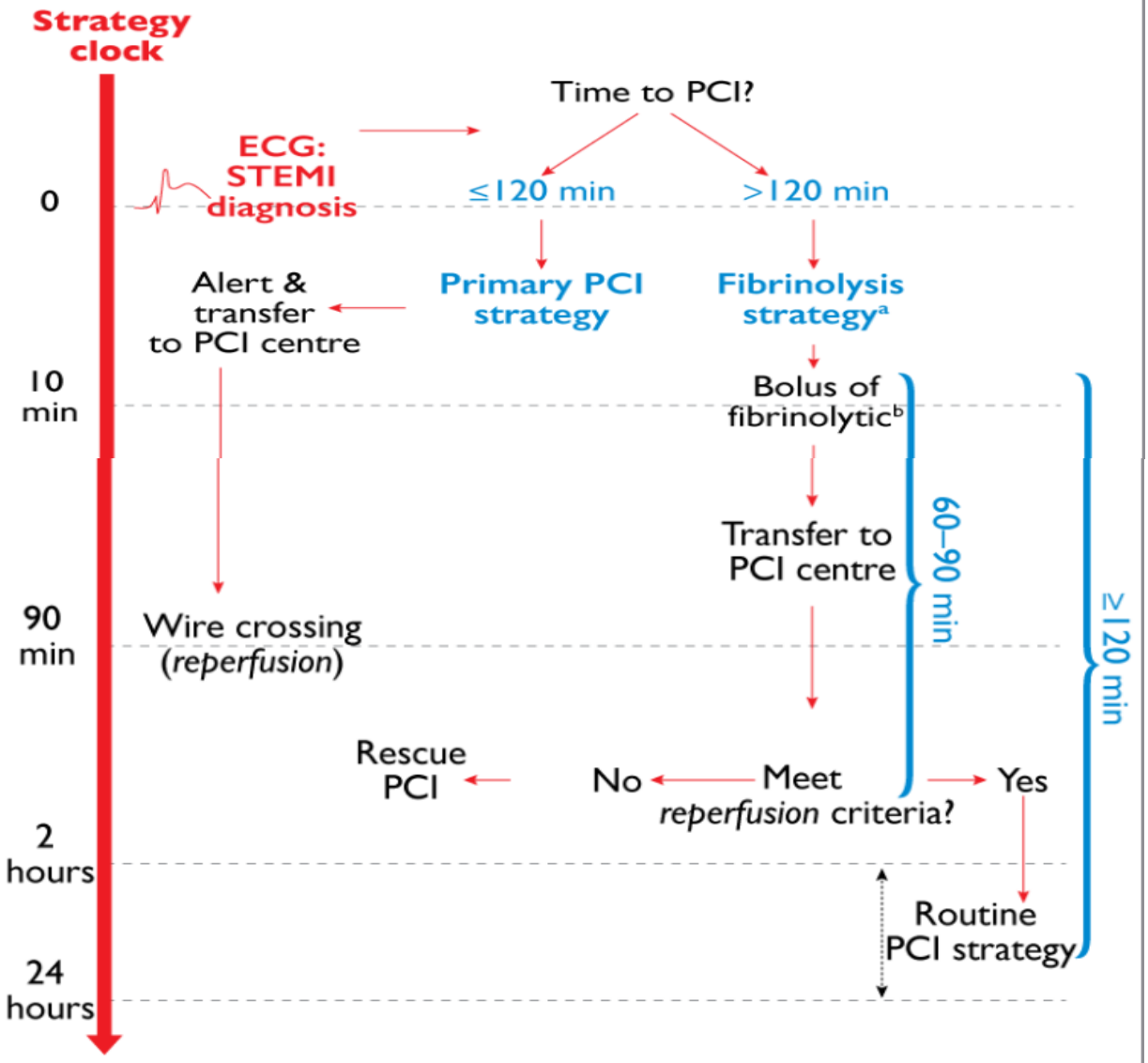
Primary PCI is the preferred reperfusion strategy in patients with STEMI within 12 h of symptom onset, provided it can be performed expeditiously (i.e. 120 min from STEMI diagnosis) by an experienced team. An experienced team includes not only interventional cardiologists but also skilled support staff.

The extent to which the PCI-related time delay diminishes the advantages of PCI over fibrinolysis has been widely debated. There is a lack of contemporaneous data to set the limit to choose PCI over fibrinolysis. For simplicity, an absolute time (120 min) from STEMI diagnosis to PCI-mediated reperfusion (i.e. wire crossing of the infarct-related artery (IRA)) rather than a relative PCI-related delay over fibrinolysis has been chosen. If the reperfusion strategy is fibrinolysis, the goal is to inject the bolus of fibrinolytic within 10 min from STEMI diagnosis.

Table 4 Definitions of terms related to reperfusion therapy

Term	Definition
FMC	The time point when the patient is either initially assessed by a physician, paramedic, nurse or other trained EMS personnel who can obtain and interpret the ECG, and deliver initial interventions (e.g. defibrillation). FMC can be either in the pre-hospital setting or upon patient arrival at the hospital (e.g. emergency department).
STEMI diagnosis	The time at which the ECG of a patient with ischaemic symptoms is interpreted as presenting ST-segment elevation or equivalent.
Primary PCI	Emergent PCI with balloon, stent, or other approved device, performed on the IRA without previous fibrinolytic treatment.
Primary PCI strategy	Emergent coronary angiography and PCI of the IRA if indicated.
Rescue PCI	Emergent PCI performed as soon as possible in the case of failed fibrinolytic treatment.
Routine early PCI strategy after fibrinolysis	Coronary angiography, with PCI of the IRA if indicated, performed between 2 and 24 hours after successful fibrinolysis.
Pharmacoinvasive strategy	Fibrinolysis combined with rescue PCI (in case of failed fibrinolysis) or routine early PCI strategy (in case of successful fibrinolysis).

Figure 3 Maximum target times according to reperfusion strategy selection in patients presenting via EMS or in a non-PCI centre



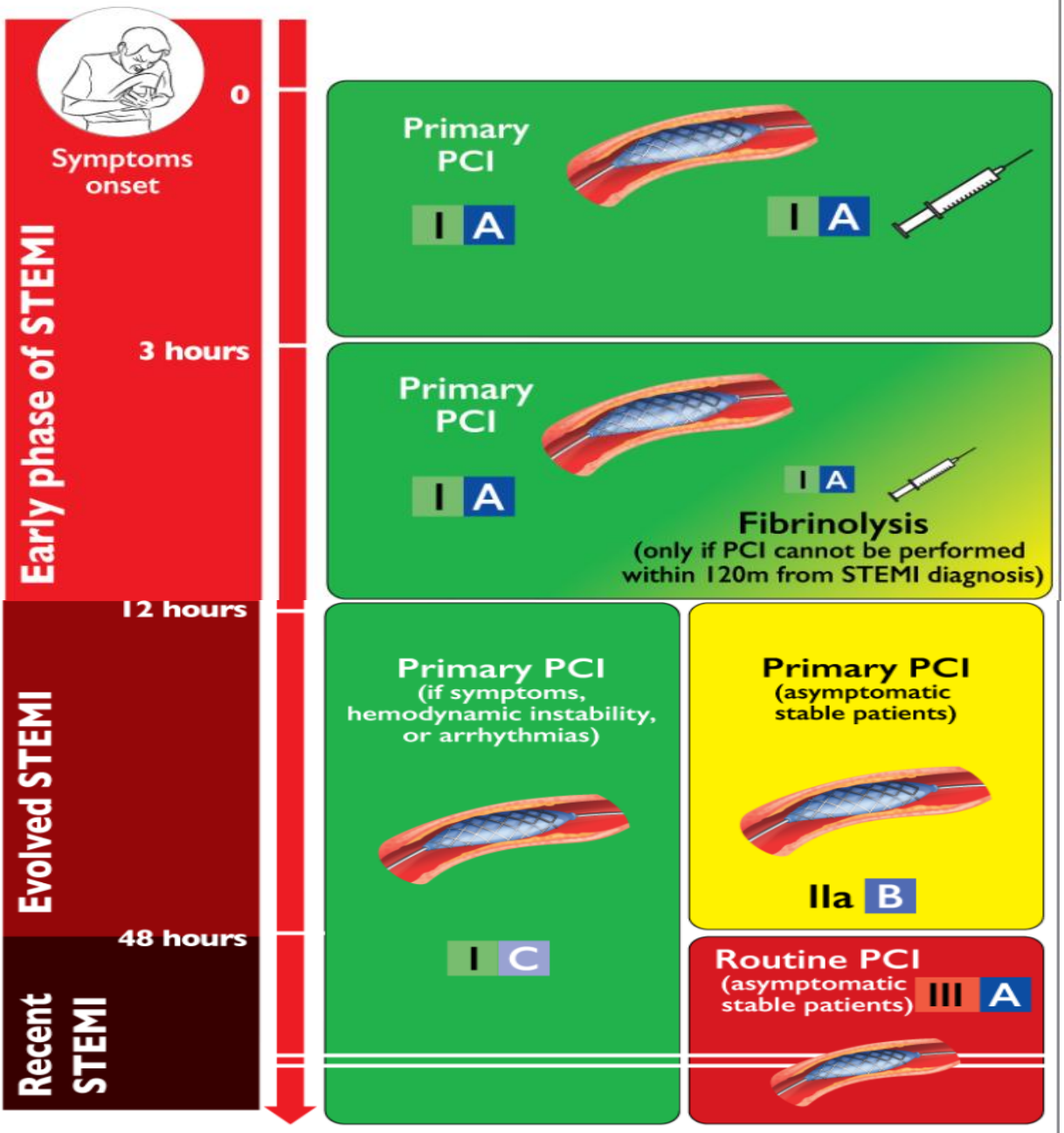
ECG = electrocardiogram; PCI = Percutaneous Coronary Intervention; STEMI = ST-segment elevation myocardial infarction.

STEMI diagnosis is the time 0 for the strategy clock. The decision for choosing reperfusion strategy in patients presenting via EMS (out-of-hospital setting) or in a non-PCI centre is based on the estimated time from STEMI diagnosis to PCI-mediated reperfusion. Target times from STEMI diagnosis represent the maximum time to do specific interventions.

[a]if fibrinolysis is contra-indicated, direct for primary PCI strategy regardless of time to PCI.

[b]10 min is the maximum target delay time from STEMI diagnosis to fibrinolytic bolus administration, however, it should be given as soon as possible after STEMI diagnosis (after ruling out contra-indications).

Figure 4 Reperfusion strategies in the infarct-related artery according to time from symptoms onset.

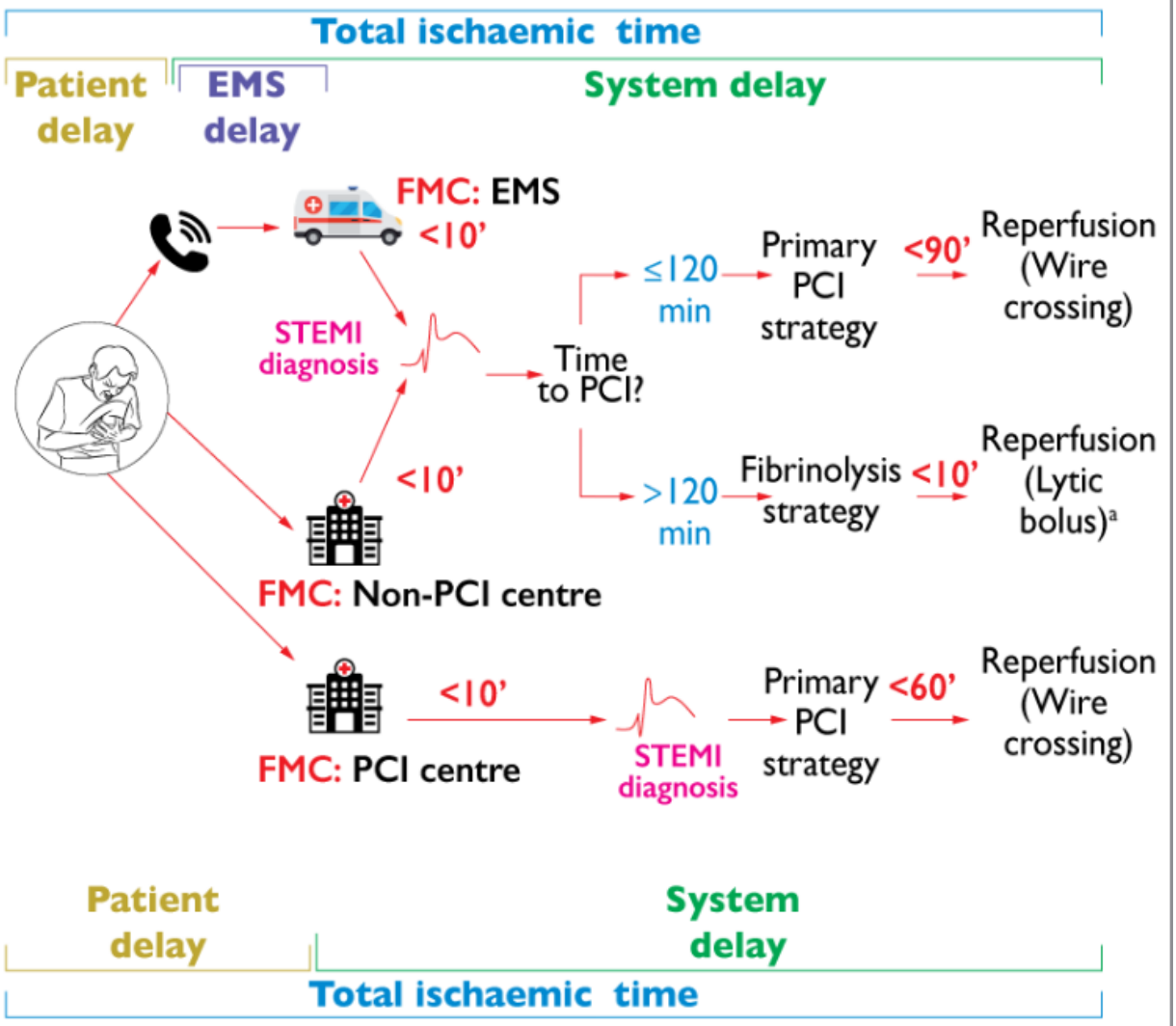


IRA = infarct-related artery; PCI = percutaneous coronary intervention; STEMI = ST-elevation myocardial infarction.

In early presenters (i.e. those with STEMI diagnosis within 3 hours from symptoms onset), a primary PCI strategy is the reperfusion strategy of choice. If the anticipated time from STEMI diagnosis to PCI-mediated reperfusion is >120 min, then immediate fibrinolysis is indicated. After 3 hours (and up to 12 hours) of symptoms onset, the later the patient presents, the more consideration should be given to a primary PCI strategy as opposed to administering fibrinolytic therapy. In evolved STEMI (12–48 hours after symptoms onset), a routine primary PCI strategy (angiography and subsequent PCI if indicated) should be considered in all patients. After 48 hours (recent STEMI) angiography should be performed but routine PCI of a total occluded IRA is not recommended. Regardless of the time from symptoms onset, the presence of ongoing symptoms suggestive of ischaemia, haemodynamic instability, or life-threatening arrhythmias is an indication for a primary PCI strategy.

Recommendations for reperfusion therapy		
Recommendations	**Class[a]**	**Level[b]**
Reperfusion therapy is indicated in all patients with symptoms of ischaemia of ≤12 hours duration and persistent ST-segment elevation.	I	A
A *primary PCI strategy* is recommended over fibrinolysis within indicated timeframes.	I	A
If timely primary PCI cannot be performed timely after STEMI diagnosis, fibrinolytic therapy is recommended within 12 hours of symptom onset in patients without contra-indications.	I	A
In the absence of ST-segment elevation, a *primary PCI strategy* is indicated in patients with suspected ongoing ischaemic symptoms suggestive of myocardial infarction and at least one of the following criteria present: • haemodynamic instability or cardiogenic shock • recurrent or ongoing chest pain refractory to medical treatment • life-threatening arrhythmias or cardiac arrest • mechanical complications of myocardial infarction • acute heart failure • recurrent dynamic ST-segment or T-wave changes, particularly with intermittent ST-segment elevation.	I	C
Early angiography (within 24 hours) is recommended if symptoms are completely relieved and ST-segment elevation completely normalized spontaneously or after nitroglycerin administration (provided there are no recurrence of symptoms or ST-segment elevation).	I	C
In patients with time from symptom onset >12 hours, a *primary PCI strategy* is indicated in the presence of ongoing symptoms suggestive of ischaemia, haemodynamic instability, or life-threatening arrhythmias.	I	C
A routine *primary PCI strategy* should be considered in patients presenting late (12–48 hours) after symptom onset.	IIa	B
In asymptomatic patients, routine PCI of an occluded IRA >48 hours after onset of STEMI is not indicated.	III	A

Figure 2 Modes of patient presentation, components of ischaemic time and flowchart for reperfusion strategy selection



The recommended mode of patient presentation is by alerting the EMS (call national emergency number: 112 or similar number according to region). When STEMI diagnosis is made in the out-of-hospital setting (via EMS) or in a non-PCI centre, the decision for choosing reperfusion strategy is based on the estimated time from STEMI diagnosis to PCI-mediated reperfusion (wire crossing). System delay for patients alerting the EMS starts at the time of phone alert, although FMC occurs when EMS arrives to the scene (see table 4 for definition of terms).

'denotes minutes.

[a]Patients with fibrinolysis should be transferred to a PCI centre immediately after administration of the lytic bolus.

Table 5 Summary of important time targets	
Intervals	**Time targets**
Maximum time from FMC to ECG and diagnosis[a]	≤10 min
Maximum expected delay from STEMI diagnosis to primary PCI (wire crossing) to choose primary PCI strategy over fibrinolysis (if this target time cannot be met, consider fibrinolysis).	≤120 min
Maximum time from STEMI diagnosis to wire crossing in patients presenting at primary PCI hospitals.	≤60 min
Maximum time from STEMI diagnosis to wire crossing in transferred patients.	≤90 min
Maximum time from STEMI diagnosis to bolus or infusion start of fibrinoly sis in patients unable to meet primary PCI target times.	≤10 min
Time delay from start of fibrinolysis to evaluation of its efficacy (success or failure).	60–90 min
Time delay from start of fibrinolysis to angiography (if fibrinolysis is successful).	2–24 hours

There is robust evidence in favour of the radial approach as the default access site in ACS patients undergoing primary PCI by experienced radial operators. Second generation DES are the stent of choice in primary PCI setting. Revascularization of non-IRA lesions should be considered in STEMI patients with multivessel disease before hospital discharge. As the optimal timing of revascularization (immediate vs. staged) has not been adequately investigated, no recommendation in favour of immediate versus staged multivessel PCI can be formulated.

Procedural aspects of the primary percutaneous coronary intervention strategy

Recommendations	Class[a]	Level[b]
IRA strategy		
Primary PCI of the IRA is indicated.	I	A
New coronary angiography with PCI if indicated is recommended in patients with symptoms or signs of recurrent or remaining ischaemia after primary PCI.	I	C
IRA technique		
Stenting is recommended (over balloon angioplasty) for primary PCI.	I	A
Stenting with new-generation DES is recommended over BMS for primary PCI.	I	A
Radial access is recommended over femoral access if performed by an experienced radial operator.	I	A
Routine use of thrombus aspiration is not recommended.	III	A
Routine use of deferred stenting is not recommended.	III	B
Non-IRA strategy		
Routine revascularization of non-IRA lesions should be considered in STEMI patients with multivessel disease before hospital discharge.	IIa	A
Non-IRA PCI during the index procedure should be considered in patients with cardiogenic shock.	IIa	C
CABG should be considered in patients with ongoing ischaemia and large areas of jeopardized myocardium if PCI of the IRA cannot be performed.	IIa	C

Patients undergoing primary PCI should receive DAPT (dual anti-platelet therapy), a combination of aspirin and a $P2Y_{12}$ inhibitor, and a parenteral anticoagulant. Routine post-procedural anticoagulant therapy is not indicated after primary PCI, except when there is a separate indication for either full-dose anticoagulation.

Periprocedural and post-procedural antithrombotic therapy[c] in patients undergoing primary percutaneous coronary intervention		
Recommendations	**Class[a]**	**Level[b]**
Antiplatelet therapy		
A potent $P2Y_{12}$ inhibitor (prasugrel or ticagrelor), or clopidogrel if these are not available or are contra-indicated, is recommended before (or at latest at the time of) PCI and maintained over 12 months unless there are contra-indications such as excessive risk of bleeding.	I	A
Aspirin (oral or i.v, if unable to swallow) is recommended as soon as possible for all patients without contra-indications.	I	B
GP IIb/IIIa inhibitors should be considered for bailout if there is evidence of no-reflow or a thrombotic complication.	IIa	C
Cangrelor may be considered in patients who have not received $P2Y_{12}$ receptor inhibitors.	IIb	A
Anticoagulant therapy		
Anticoagulation is recommended for all patients in addition to antiplatelet therapy during primary PCI.	I	C
Routine use of UFH is recommended.	I	C
In patients with heparin-induced thrombocytopenia, bivalirudin is recommended as the anticoagulant agent during primary PCI.	I	C
Routine use of enoxaparin *i.v.* should be considered.	IIa	A
Routine use of bivalirudin should be considered.	IIa	A
Fondaparinux is not recommended for primary PCI.	III	B

Table 6 Doses of antiplatelet and anticoagulant co-therapies in patients undergoing primary percutaneous coronary intervention or not reperfused	
Doses of antiplatelet and parenteral anticoagulant co-therapies in primary PCI	
Antiplatelet therapies	
Aspirin	Loading dose of 150–300 mg orally or of 75–250 mg *i.v.* if oral ingestion is not possible, followed by a maintenance dose of 75–100 mg/day.
Clopidogrel	Loading dose of 600 mg orally, followed by a maintenance dose of 75 mg/day.
Prasugrel	Loading dose of 60 mg orally, followed by a maintenance dose of 10 mg/day In patients with body weight ≤60 kg, a maintenance dose of 5 mg/day is recommended. Prasugrel is contra-indicated in patients with previous stroke. In patients ≥75 years, prasugrel is generally not recommended, but a dose of 5 mg/day should be used if treatment is deemed necessary.
Ticagrelor	Loading dose of 180 mg orally, followed by a maintenance dose of 90 mg *b.i.d.*
Abciximab	Bolus of 0.25 mg/kg *i.v.* and 0.125 μg/kg/min infusion (maximum 10 μg/min) for 12 hours.
Eptifibatide	Double bolus of 180 μg/kg *i.v.* (given at a 10-min interval) followed by an infusion of 2.0 μg/kg/min for up to 18 hours.
Tirofiban	25 μg/kg over 3 min *i.v.*, followed by a maintenance infusion of 0.15 μg/kg/min for up to 18 hours.
Parenteral anticoagulant therapies	
UFH	70–100 IU/kg *i.v.* bolus when no GP IIb/IIIa inhibitor is planned 50–70 IU/kg *i.v.* bolus with GP IIb/IIIa inhibitors.
Enoxaparin	0.5 mg/kg *i.v.* bolus.
Bivalirudin	0.75 mg/kg *i.v.* bolus followed by *i.v.* infusion of 1.75 mg/kg/hour for up to hours after the procedure.
Doses of antiplatelet and parenteral anticoagulant therapies in patients not receiving reperfusion therapy	
Antiplatelet therapies	
Aspirin	Loading dose of 150–300 mg orally followed by a maintenance dose of 75–100 mg/day.
Clopidogrel	Loading dose of 300 mg orally, followed by a maintenance dose of 75 mg/day orally.
Parenteral anticoagulant therapies	
UFH	Same dose as with fibrinolytic therapy (see Table 7).
Enoxaparin	Same dose as with fibrinolytic therapy (see Table 7).
Fondaparinux	Same dose as with fibrinolytic therapy (see Table 7).

Fibrinolytic therapy is an important reperfusion strategy in settings where primary PCI cannot be offered in a timely manner. In the presence of contra-indications for fibrinolytic treatment it is important to weigh the potentially lifesaving effect of fibrinolysis against potentially life-threatening side effects taking into account alternative treatment options such as delayed primary PCI.

If trained medical or paramedical staff are able to analyse the ECG on-site or to transmit the ECG to the hospital for interpretation, it is recommended to initiate fibrinolytic therapy in the pre-hospital setting. The aim is to start fibrinolytic therapy within 10 min from STEMI diagnosis.

Following initiation of lytic therapy, it is recommended to transfer the patients to a PCI centre. In cases of failed fibrinolysis, or if there is evidence of reocclusion or reinfarction with recurrence of ST-segment elevation, immediate angiography and rescue PCI is indicated. Re-administration of fibrinolysis should be discouraged. Even if it is likely that fibrinolysis will be successful, a strategy of routine early angiography (2-24h after fibrinolysis) is recommended if there are no contraindications.

Weight-adjusted *i.v.* tenecteplase, aspirin and clopidogrel given orally, and enoxaparin *i.v.* followed by *s.c.* administration until the time of PCI (revascularization), comprise the antithrombotic cocktail most extensively studied.

Fibrinolytic therapy		
Recommendations	**Class[a]**	**Level[b]**
When fibrinolysis is the reperfusion strategy, it is recommended to initiate this treatment as soon as possible after STEMI diagnosis, preferably in the pre-hospital setting.	I	A
A fibrin-specific agent (i.e. tenecteplase, alteplase, reteplase) is recommended.	I	B
A half-dose of tenecteplase should be considered in patients ≥75 years of age.	IIa	B
Antiplatelet co-therapy with fibrinolysis		
Oral or *i.v.* aspirin is indicated.	I	B
Clopidogrel is indicated in addition to aspirin.	I	A
DAPT (in the form of aspirin plus a $P2Y_{12}$ inhibitor[c]) is indicated for up to 1 year in patients undergoing fibrinolysis and subsequent PCI.	I	C
Anticoagulation co-therapy with fibrinolysis		
Anticoagulation is recommended in patients treated with lytics until revascularization (if performed) or for the duration of hospital stay up to 8 days.The anticoagulant can be:	I	A
• Enoxaparin *i.v.* followed by *s.c.* (preferred over UFH).	I	A
• UFH given as a weight-adjusted *i.v.* bolus followed by infusion.	I	B
• In patients treated with streptokinase: fondaparinux *i.v.* bolus followed by a *s.c.* dose 24 hours later.	IIa	B
Transfer after fibrinolysis		
Transfer to a PCI-capable centre following fibrinolysis is indicated in all patients immediately after fibrinolysis.	I	A

Interventions following fibrinolysis		
Emergency angiography and PCI if indicated is recommended in patients with heart failure/shock.	I	A
Rescue PCI is indicated immediately when fibrinolysis has failed (< 50% ST-segment resolution at 60–90 min) or at any time in the presence of haemodynamic or electrical instability, or worsening ischaemia.	I	A
Angiography and PCI of the IRA, if indicated, is recommended between 2 and 24 hours after successful fibrinolysis.	I	A
Emergency angiography and PCI if needed is indicated in the case of recurrent ischaemia or evidence of reocclusion after initial successful fibrinolysis.	I	B

DAPT = dual antiplatelet therapy; IRA = infarct-related artery; *i.v.* = intravenous; PCI = percutaneous coronary intervention; SBP = systolic blood pressure; *s.c.* = subcutaneous; STEMI = ST-segment elevation myocardial infarction; UFH = unfractionated heparin.

[a]Class of recommendation - [b]Level of evidence.

[c]Clopidogrel is the $P2Y_{12}$ inhibitor of choice as co-adjuvant and after fibrinolysis, 48 hours after fibrinolysis, switch to prasugrel/ticagrelor may be considered in patients who underwent PCI.

Doses of agents at fibrinolysis

Doses of fibrinolytic agents and antithrombotic co-therapies are listed in Table 7.

Table 7 Doses of fibrinolytic agents and antithrombotic co-therapies

Drug	Initial treatment	Specific contra-indications
Doses of fibrinolytic therapy		
Streptokinase	1.5 million units over 30–60 min *i.v.*	Previous treatment with streptokinase or anistreplase
Alteplase (tPA)	15 mg *i.v.* bolus 0.75 mg/kg *i.v.* over 30 min (up to 50 mg) then 0.5 mg/kg *i.v.* over 60 min (up to 35 mg)	
Reteplase (rPA)	10 units + 10 units *i.v.* bolus given 30 min apart	
Tenecteplase (TNK-tPA)	Single *i.v.* bolus: 30 mg (6000 IU) if <60 kg 35 mg (7000 IU) if 60 to <70 kg 40 mg (8000 IU) if 70 to <80 kg 45 mg (9000 IU) if 80 to <90 kg 50 mg (10000 IU) if ≥ 90 kg It is recommended to reduce to half-dose in patients ≥75 years of age.	

Doses of antiplatelet co-therapies		
Aspirin	Starting dose of 150–300 mg orally (or 75–250 mg intravenously if oral ingestion is not possible), followed by a maintenance dose of 75–100 mg/day.	
Clopidogrel	Loading dose of 300 mg orally, followed by a maintenance dose of 75 mg/day. In patients ≥75 years of age: loading dose of 75 mg, followed by a maintenance dose of 75 mg/day.	
Doses of anticoagulant co-therapies		
Enoxaparin	In patients <75 years of age: 30 mg *i.v.* bolus followed 15 min later by 1 mg/kg *s.c.* every 12 hours until revascularization or hospital discharge for a maximum of 8 days.The first two *s.c.* doses should not exceed 100 mg per injection.	
	In patients ≥ 75 years of age: no *i.v.* bolus; start with first *s.c.* dose of 0.75 mg/kg with a maximum of 75 mg per injection for the first two *s.c.* doses. In patients with eGFR <30 mL/min/1.73 m^2, regardless of age, the *s.c.* doses are given once every 24 hours.	
UFH	60 IU/kg *i.v.* bolus with a maximum of 4000 IU followed by an *i.v.* infusion of 12 IU/kg with a maximum of 1000 IU/hour for 24–48 hours. Target aPTT: 50–70 s or 1.5 to 2.0 times that of control to be monitored at 3, 6, 12 and 24 hours.	
Fondaparinux (only with streptokinase)	2.5 mg *i.v.* bolus followed by a *s.c.* dose of 2.5 mg once daily up to 8 days or hospital discharge.	

aPTT = activated partial thromboplastin time; eGFR = estimated glomerular filtration rate; *i.v.* = intravenous; IU = international units; rPA = recombinant plasminogen activator; *s.c.* = subcutaneous; tPA = tissue plasminogen activator; UFH = unfractionated heparin.

Table 8 Contra-indications to fibrinolytic therapy
Absolute
Previous intracranial haemorrhage or stroke of unknown origin at anytime.
Ischaemic stroke in the preceding 6 months.
Central nervous system damage or neoplasms or arteriovenous malformation.
Recent major trauma/surgery/head injury (within the preceding month).
Gastrointestinal bleeding within the past month.
Known bleeding disorder (excluding menses).
Aortic dissection.
Non-compressible punctures in the past 24 hours (e.g. liver biopsy, lumbar puncture).
Relative
Transient ischaemic attack in the preceding 6 months.
Oral anticoagulant therapy.
Pregnancy or within 1 week postpartum.
Refractory hypertension (SBP >180 mmHg and/or DBP >110 mmHg).
Advanced liver disease.
Infective endocarditis.
Active peptic ulcer.
Prolonged or traumatic resuscitation.

AV = arteriovenous; DBP = diastolic blood pressure; SBP = systolic blood pressure.

Emergent CABG should be considered for patients with a patent IRA but with unsuitable anatomy for PCI and either a large myocardial area at jeopardy or with cardiogenic shock. In patients with myocardial infarction-related mechanical complications who require coronary revascularization, CABG is recommended at the time of repair.

Optimal timing for non-emergent CABG in stabilized post- myocardial infarction patients should be determined individually. Patients with haemodynamic deterioration or who are at high-risk of recurrent ischaemic events (i.e. patients with large area of myocardium at jeopardy due to critical coronary stenoses or recurrent ischaemia) should be operated on as soon as possible without waiting for the full recovery of platelet function following discontinuation of DAPT. For all other patients, a waiting period of 3–7 days may be the best compromise, while it is recommended to continue aspirin. The first aspirin administration post-CABG is recommended 6–24 h after surgery in the absence of ongoing bleeding events.

Logistical issues for hospital stay		
Recommendations	**Class[a]**	**Level[b]**
It is indicated that all hospitals participating in the care of STEMI patients have a CCU/ICCU equipped to provide all aspects of care for STEMI patients, including treatment of ischaemia, severe heart failure, arrhythmias, and common comorbidities.	I	C
Transfer back to a referring non-PCI hospital		
Same-day transfer should be considered appropriate in selected patients after successful primary PCI, i.e. those without ongoing myocardial ischaemia, arrhythmia, or haemodynamic instability, not requiring vasoactive or mechanical support, and not needing further early revascularization.	IIa	C
Monitoring		
It is indicated that all STEMI patients have ECG monitoring for a minimum of 24 hours.	I	C
Length of stay in the CCU		
It is indicated that patients with successful reperfusion therapy and uncomplicated clinical course are kept in the CCU/ICCU for a minimum of 24 hours whenever possible, after which they may be moved to a step-down monitored bed for an additional 24–48 hours.	I	C
Hospital discharge		
Early discharge (within 48–72 hours) should be considered appropriate in selected low-risk patients[c] if early rehabilitation and adequate follow-up are arranged.	IIa	A

CCU = coronary care unit; ICCU = intensive cardiac care unit; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

[a]Class of recommendation - [b]Level of evidence - [c]For example, Second Primary Angioplasty in Myocardial Infarction (PAMI-II) criteria: age <70 years, LVEF >45%, one- or two-vessel disease, successful PCI and no persistent arrhythmias.

Special patient subsets

Patients taking oral anticoagulation

Many patients presenting with STEMI are previously on oral anticoagulation or require long-term anticoagulation afterwards.

Management during STEMI: Patients taking oral anticoagulation should be triaged for primary PCI strategy regardless of the anticipated time to PCI-mediated reperfusion. Patients should receive additional parenteral anticoagulation, regardless of the timing of the last dose of oral anticoagulant. Loading of aspirin should be done as in all STEMI patients, and clopidogrel is the $P2Y_{12}$ inhibitor of choice (600 mg loading dose) before or at the latest at the time of PCI. Chronic anticoagulation regimen should not be stopped during admission. Gastric protection with a proton pump inhibitor (PPI) is recommended.

Maintenance after STEMI: Triple therapy (oral anticoagulation, aspirin and clopidogrel) should be considered for 6 months. Then, oral anticoagulation plus aspirin or clopidogrel should be considered for additional 6 months. After 1 year it is indicated to maintain only oral anticoagulation.

Elderly patients

Owing to the ageing of the population, a higher proportion of elderly patients is expected to present with STEMI. As these patients may present with atypical symptoms, the diagnosis of myocardial infarction may be delayed or missed. Elderly patients are also at particular risk of bleeding and other complications. It is, therefore, key to treat them as recommended and using specific strategies to reduce bleeding risk; these include paying attention to proper dosing of antithrombotic therapies.

Renal dysfunction

The type and dose of antithrombotic agent and the amount of contrast agent should be considered based on renal function. ACS patients with chronic kidney disease (CKD) receive frequently excess dosing with antithrombotics, contributing to the increased bleeding risk. Ensuring proper hydration during and after primary PCI and limiting the dose of contrast agents, preferentially low - osmolality contrast agents, are important steps in minimizing the risk of contrast-induced nephropathy.

Table 9: Recommended doses of antithrombotic agents in the acute care of patients with chronic kidney

Aspirin	
Normal renal function and stage 1–3 CKD (eGFR ≥30 mL/min/1.73 m^2)	Loading dose of 150–300 mg orally followed by a maintenance dose of 75–100 mg/day.
Stage 4 CKD (eGFR 15 to <30 mL/min/1.73 m^2)	No dose adjustment
Stage 5 CKD (eGFR <15 mL/min/1.73 m^2)	No dose adjustment
Clopidogrel	
Normal renal function and stage 1–3 CKD (eGFR ≥30 mL/min/1.73 m^2)	Loading dose of 300–600 mg orally followed by 75 mg/day.
Stage 4 CKD (eGFR 15 to <30 mL/min/1.73 m^2)	No dose adjustment
Stage 5 CKD (eGFR <15 mL/min/1.73 m^2)	No information available

Ticagrelor	
Normal renal function and stage 1–3 CKD (eGFR ≥30 mL/min/1.73 m^2)	Loading dose of 180 mg orally followed 90 mg twice a day.
Stage 4 CKD (eGFR 15 to <30 mL/min/1.73 m^2)	No dose adjustment
Stage 5 CKD (eGFR <15 mL/min/1.73 m^2)	Not recommended
Prasugrel	
Normal renal function and stage 1–3 CKD (eGFR ≥30 mL/min/1.73 m^2)	Loading dose of 60 mg orally followed by 10 mg/ day.
Stage 4 CKD (eGFR 15 to <30 mL/min/1.73 m^2)	No dose adjustment
Stage 5 CKD (eGFR <15 mL/min/1.73 m^2)	Not recommended
Enoxaparin	
Normal renal function and stage 1–3 CKD (eGFR ≥30 mL/min/1.73 m^2)	1 mg/kg *s.c.* twice a day, 0.75 mg/kg *s.c.* twice daily in patients ≥75 years old.
Stage 4 CKD (eGFR 15 to <30 mL/min/1.73 m^2)	1 mg/kg *s.c.* once a day
Stage 5 CKD (eGFR <15 mL/min/1.73 m^2)	Not recommended
UFH	
Normal renal function and stage 1–3 CKD (eGFR ≥30 mL/min/1.73 m^2)	*Before coronary angiography:* Bolus 60–70 IU/kg *i.v.* (maximum 5000 IU) and infusion (12–15 IU/kg/hour, maximum 1000 IU/ hour), target aPTT 1.5–2.5 x control. *During PCI:* 70-100 IU/kg *i.v.* (50-70 IU/kg if concomitant with GP IIb/IIIa inhibitors).
Stage 4 CKD (eGFR 15 to <30 mL/min/1.73 m^2)	No dose adjustment
Stage 5 CKD (eGFR <15 mL/min/1.73 m^2)	No dose adjustment
Fondaparinux	
Normal renal function and stage 1–3 CKD (eGFR ≥30 mL/min/1.73 m^2)	2.5 mg *s.c.* once a day.
Stage 4 CKD (eGFR 15 to <30 mL/min/1.73 m^2)	Not recommended if eGFR <20 mL/min/1.73 m^2 or dialysis
Stage 5 CKD (eGFR <15 mL/min/1.73 m^2)	Not recommended

Bivalirudin	
Normal renal function and stage 1–3 CKD (eGFR ≥30 mL/min/1.73 m^2)	Bolus 0.75 mg/kg *i.v.*, infusion 1.75 mg/kg/hour. *If eGFR ≥30 and ≤60 mL/min/1.73m^2 reduce infusion dose to 1.4 mg/kg/hour.*
Stage 4 CKD (eGFR 15 to <30 mL/min/1.73 m^2)	Not recommended
Stage 5 CKD (eGFR <15 mL/min/1.73 m^2)	Not recommended
Abciximab	
Normal renal function and stage 1–3 CKD (eGFR ≥30 mL/min/1.73 m^2)	Bolus of 0.25 mg/kg *i.v.* followed by 0.125 µg/kg/min infusion (maximum 10 µg/min).
Stage 4 CKD (eGFR 15 to <30 mL/min/1.73 m^2)	Careful consideration of bleeding risk
Stage 5 CKD (eGFR <15 mL/min/1.73 m^2)	Careful consideration of bleeding risk
Eptifibatide	
Normal renal function and stage 1–3 CKD (eGFR ≥30 mL/min/1.73 m^2)	Bolus[a] of 180 µg/kg *i.v.* followed by an infusion of 2.0 µg/kg/min for up to 18 hours. If eGFR <50 mL/min/1.73 m^2 reduce infusion dose to 1.0 µg/kg/min.
Stage 4 CKD (eGFR 15 to <30 mL/min/1.73 m^2)	Not recommended
Stage 5 CKD (eGFR <15 mL/min/1.73 m^2)	Not recommended
Tirofiban	
Normal renal function and stage 1–3 CKD (eGFR ≥30 mL/min/1.73 m^2)	Bolus 25 µg/kg *i.v.* followed by 0.15 µg/kg/min.
Stage 4 CKD (eGFR 15 to <30 mL/min/1.73 m^2)	Reduce infusion rate to 50%
Stage 5 CKD (eGFR <15 mL/min/1.73 m^2)	Not recommended

aPTT = activated partial thromboplastin time; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; GP = glycoprotein; IU = international units; *i.v.* = intravenous; PCI = percutaneous coronary intervention; *s.c.* = subcutaneous; UFH = unfractionated heparin.

[a]Double bolus if administered during primary PCI.

Management of hyperglycaemia

Recommendations	Class[a]	Level[b]
It is recommended to measure glycaemic status at initial evaluation in all patients, and perform frequent monitoring in patients with known diabetes or hyperglycaemia (defined as glucose levels ≥11.1 mmol/L or ≥200 mg/dL).	I	C
In patients on metformin and/or SGLT2 inhibitors, renal function should be carefully monitored for at least 3 days after coronary angiography/PCI.[c]	I	C
Glucose-lowering therapy should be considered in ACS patients with glucose levels >10 mmol/L (>180 mg/dL), while episodes of hypoglycaemia (defined as glucose levels ≤ 3.9 mmol/L or ≤70 mg/dL) should be avoided.	IIa	C
Less stringent glucose control should be considered in the acute phase in patients with more advanced cardiovascular disease, older age, longer diabetes duration, and more comorbidities.	IIa	C

ACS = acute coronary syndrome; PCI = percutaneous coronary intervention; SGLT2 = sodium-glucose cotransporter-2.

[a]Class of recommendation - [b]Level of evidence.

[c]A short withdrawal of metformin may be considered after an invasive coronary procedure.

All STEMI patients should have an early assessment of short-term risk, including an evaluation of the extent of myocardial damage, the occurrence of successful reperfusion, and the presence of clinical markers of high-risk of further events.

Routine echocardiography after primary PCI is recommended to assess resting LV function, as well as RV and valve function, to exclude early post-infarction mechanical complications and LV thrombus.

Summary of indications for imaging and stress testing in ST-elevation myocardial infarction patients		
Recommendations	**Class[a]**	**Level[b]**
At presentation		
Emergency echocardiography is indicated in patients with cardiogenic shock and/or haemodynamic instability or suspected mechanical complications without delaying angiography.	I	C
Emergency echocardiography before coronary angiography should be considered if the diagnosis is uncertain.	IIa	C
Routine echocardiography that delays emergency angiography is not recommended.	III	C
Coronary CT angiography is not recommended.	III	C
During hospital stay (after primary PCI)		
Routine echocardiography to assess resting LV and RV function, detect early post-MI mechanical complications, and exclude LV thrombus is recommended in all patients.	I	B
Emergency echocardiography is indicated in haemodynamically unstable patients.	I	C
When echocardiography is suboptimal/inconclusive, an alternative imaging method (CMR preferably) should be considered.	IIa	C
Either stress echo, CMR, SPECT, or PET may be used to assess myocardial ischaemia and viability, including in multivessel CAD.	IIb	C
After discharge		
In patients with pre-discharge LVEF ≤40%, repeat echocardiography 6–12 weeks after MI, and after complete revascularization and optimal medical therapy, is recommended to assess the potential need for primary prevention ICD implantation.	I	C
When echo is suboptimal or inconclusive, alternative imaging methods (CMR preferably) should be considered to assess LV function.	IIa	C

CAD = coronary artery disease; CMR = cardiac magnetic resonance; CT = computed tomography; ICD = implantable cardioverter defibrillator; LV = left ventricular; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention; PET = positron emission tomography; RV = right ventricular; SPECT = single-photon emission computed tomography.

Key lifestyle interventions include cessation of smoking, optimal blood pressure control, diet advice and weight control, and encouraging physical activity. Low treatment adherence is an important barrier to achieving optimal treatment targets and is associated with worse outcomes. Delayed outpatient follow-up after AMI results in worse short- and long-term medication adherence. Healthcare professionals and patients should be aware of this challenge and optimize communication by providing clear information, simplify treatment regimens, aim at shared decision-making, and implement repetitive monitoring and feedback. DAPT is recommended in STEMI patients who underwent primary PCI or fibrinolysis with subsequent PCI. For patients undergoing fibrinolysis without subsequent PCI and for those not reperfused, one month DAPT is recommended and prolongation up to 12 months should be considered.

Behavioural aspects after ST-elevation myocardial infarction

Recommendations	Class[a]	Level[b]
It is recommended to identify smokers and provide repeated advice on stopping, with offers to help with the use of follow-up support, nicotine-replacement therapies, varenicline, and bupropion individually or in combination.	I	A
Participation in a cardiac rehabilitation programme is recommended.	I	A
A smoking-cessation protocol is indicated for each hospital participating in the care of STEMI patients.	I	C
The use of the polypill and combination therapy to increase adherence to drug therapy may be considered.	IIb	B

Maintenance antithrombotic strategy after ST-elevation myocardial infarction		
Recommendations	**Class[a]**	**Level[b]**
Antiplatelet therapy with low-dose aspirin (75–100 mg) is indicated.	I	A
DAPT in the form of aspirin plus ticagrelor or prasugrel (or clopidogrel if ticagrelor or prasugrel are not available or are contra-indicated) is recommended for 12 months after PCI unless there are contra-indications such as excessive risk of bleeding.	I	A
A PPI in combination with DAPT is recommended in patients at high-risk of gastrointestinal bleeding[c].	I	B
In patients with an indication for oral anticoagulation, oral anticoagulants are indicated in addition to antiplatelet therapy.	I	C
In patients who are at high-risk of severe bleeding complications, discontinuation of $P2Y_{12}$ inhibitor therapy after 6 months should be considered.	IIa	B
In STEMI patients with stent implantation and an indication for oral anticoagulation, triple therapy[d] should be considered for 1–6 months (according to a balance between the estimated risk of recurrent coronary events and bleeding).	IIa	C
DAPT for 12 months in patients who did not undergo PCI should be considered unless there are contra-indications such as excessive risk of bleeding.	IIa	C
In patients with LV thrombus, anticoagulation should be administered for up to 6 months guided by repeated imaging.	IIa	C
In high ischaemic-risk patients[e] who have tolerated DAPT without a bleeding complication, treatment with DAPT in the form of ticagrelor 60 mg twice a day on top of aspirin for longer than 12 months may be considered for up to 3 years.	IIb	B
In low bleeding-risk patients who receive aspirin and clopidogrel, low-dose rivaroxaban (2.5 mg twice daily) may be considered.	IIb	B
The use of ticagrelor or prasugrel is not recommended as part of triple antithrombotic therapy with aspirin and oral anticoagulation.	III	C

AMI = acute myocardial infarction; CAD = coronary artery disease; DAPT = dual antiplatelet therapy;
eGFR = estimated glomerular filtration rate; LV = left ventricular; PCI = percutaneous coronary intervention; PPI = proton pump inhibitor; STEMI = ST-segment elevation myocardial infarction.
[a]Class of recommendation.
[b]Level of evidence.
[c]History of gastrointestinal bleeding, anticoagulant therapy, chronic non-steroidal anti-inflammatory drug/ corticosteroid user, and ≥2 or more of the following: age ≥65 years, dyspepsia, gastro-oesophageal reflux disease, Helicobacter pylori infection, chronic alcohol use.
[d]Oral anticoagulant, aspirin and clopidogrel.
[e]Defined as age ≥50 years, and ≥1 of the following additional high-risk features: age ≥65 years, diabetes mellitus on medication, a prior spontaneous AMI, multivessel CAD, or chronic renal dysfunction (eGFR <60 ml/min/1.73 m^2).

Routine therapies in the acute, subacute and long-term phases: beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, mineralocorticoid receptor antagonists, and lipid-lowering treatments after ST-elevation myocardial infarction

Recommendations	Class[a]	Level[b]
Beta-blockers		
Oral treatment with beta-blockers is indicated in patients with heart failure and/or LVEF ≤40% unless contra-indicated.	I	A
Intravenous beta-blockers should be considered at the time of presentation in patients undergoing primary PCI without contra-indications, with no signs of acute heart failure, and with an SBP >120 mmHg.	IIa	A
Routine oral treatment with beta-blockers should be considered during hospital stay and continued thereafter in all patients without contra-indications.	IIa	B
Intravenous beta-blockers must be avoided in patients with hypotension, acute heart failure or AV block or severe bradycardia.	III	B
Lipid lowering therapies		
It is recommended to start high-intensity statin therapy[c] as early as possible, unless contra-indicated, and maintain it long-term	I	A
An LDL-C goal of <1.8 mmol/L (70 mg/dL) or a reduction of at least 50% if the baseline LDL-C is between 1.8–3.5 mmol/L (70–135 mg/dL) is recommended.	I	B
It is recommended to obtain a lipid profile in all STEMI patients as soon as possible after presentation.	I	C

In patients with LDL-C ≥1.8 mmol/L (≥70 mg/dL) despite a maximally tolerated statin dose who remain at high-risk, further therapy to reduce LDL-C should be considered.	IIa	A
ACE-inhibitors/ARBs		
ACE-inhibitors are recommended, starting within the first 24 hours of STEMI in patients with evidence of heart failure, LV systolic dysfunction, diabetes, or an anterior infarct.	I	A
An ARB, preferably valsartan, is an alternative to ACE-inhibitors in patients with heart failure and/or LV systolic dysfunction, particularly those who are intolerant of ACE-inhibitors.	I	B
ACE-inhibitors should be considered in all patients in the absence of contra-indications.	IIa	A
MRAs		
MRAs are recommended in patients with an LVEF ≤40% and heart failure or diabetes, who are already receiving an ACE-inhibitor and a beta-blocker, provided there is no renal failure or hyperkalaemia.	I	B

AV = atrioventricular; ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; LDL-C = low-density lipoprotein cholesterol; LV = left ventricular; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid receptor antagonist; PCI = percutaneous coronary intervention; SBP = systolic blood pressure; STEMI = ST-segment elevation myocardial infarction.

[a]Class of recommendation - [b]Level of evidence - [c]High intensity statin defined as atorvastatin 40–80 mg and rosuvastatin 20–40 mg.

Mostly prescribed interventions (Class I, green, and IIa, yellow) are presented along with the expected timing of delivery. Solid lines represent recurrent (daily) intervention. Double-arrowed dashed lines represent a time-window in which the intervention can be delivered.

[1]Aspirin loading dose: 150–300 mg chewed or 75–250 mg intravenous (in patients not already on an aspirin maintenance dose).

[2]Prasugrel loading dose: 60 mg.Ticagrelor loading dose: 180 mg. If there are contra-indications for prasugrel/ticagrelor or these are not available, a loading dose of clopidogrel (600 mg) is indicated.

[3]If the interventional cardiologist is not expert in radial access, the femoral route is then preferred.

[4]Enoxaparin or bivalirudin are alternatives to unfractionated heparin (Class IIa A).

[5]Aspirin maintenance dose: 75–100 mg oral.

[6]Prasugrel maintenance dose: 10 mg once daily.Ticagrelor maintenance dose: 90 mg twice daily. If there are contra-indications for prasugrel/ticagrelor or these are not available, clopidogrel maintenance (75 mg daily) is indicated.

[a]90 min represents the maximum target time to PCI-mediated reperfusion. For patients presenting in a PCI-centre, this target time is 60 min.

[b]Prolongation of ticagrelor (60 mg twice daily) in addition to aspirin may be considered for up to 36 months in patients at high ischaemic risk who have tolerated DAPT without a bleeding complication.

Figure 5 "Do not forget" interventions in STEMI patients undergoing a primary PCI strategy

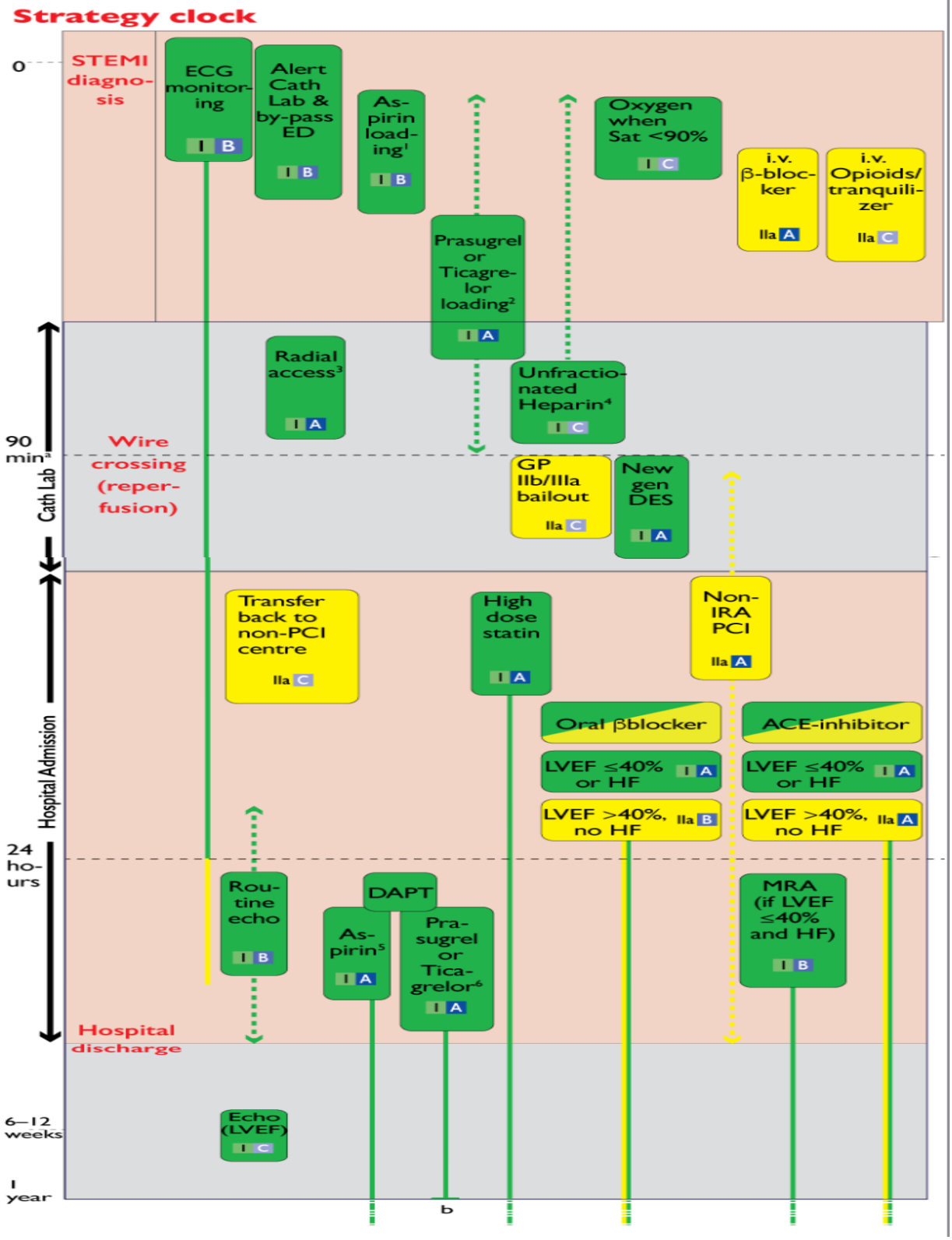
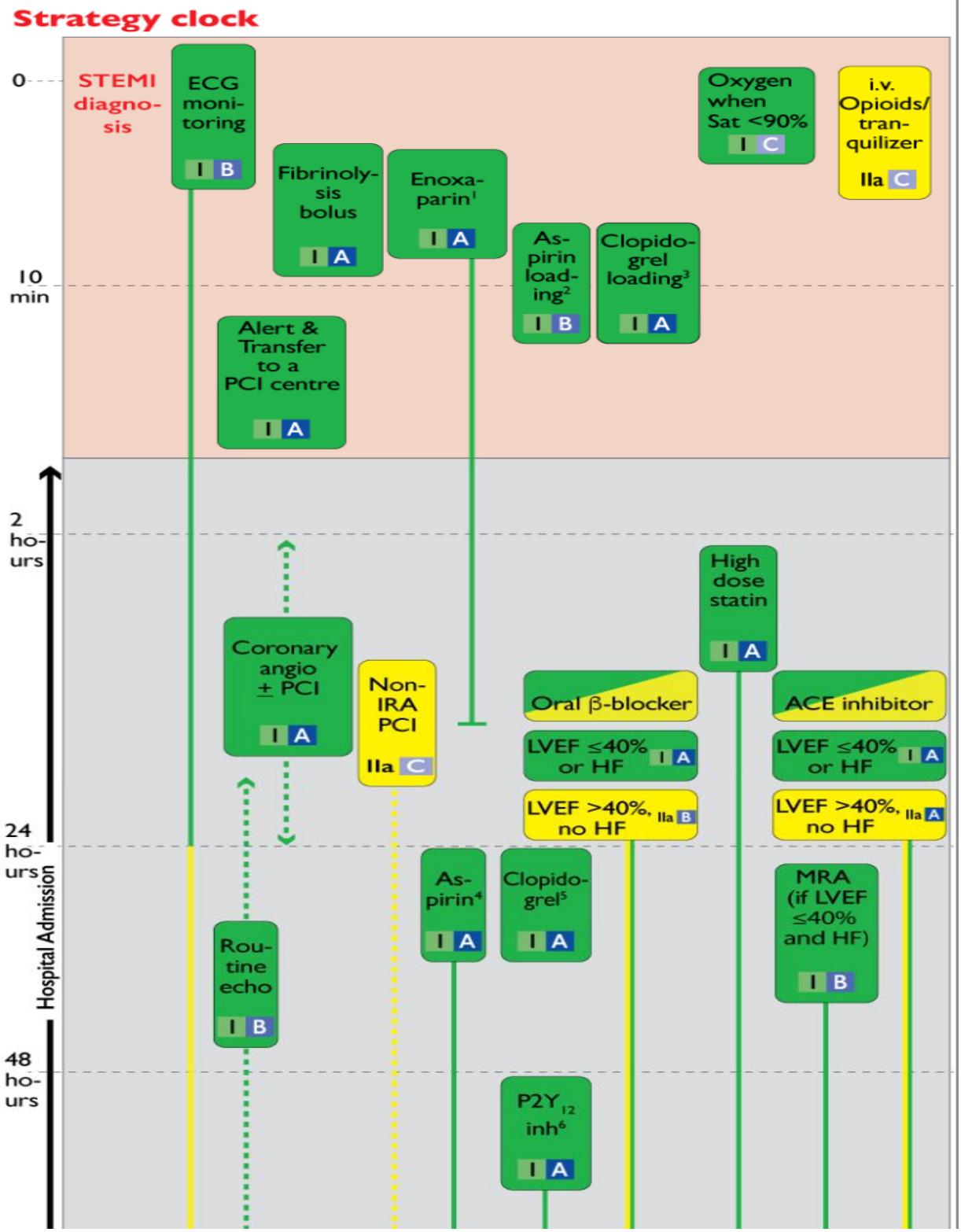
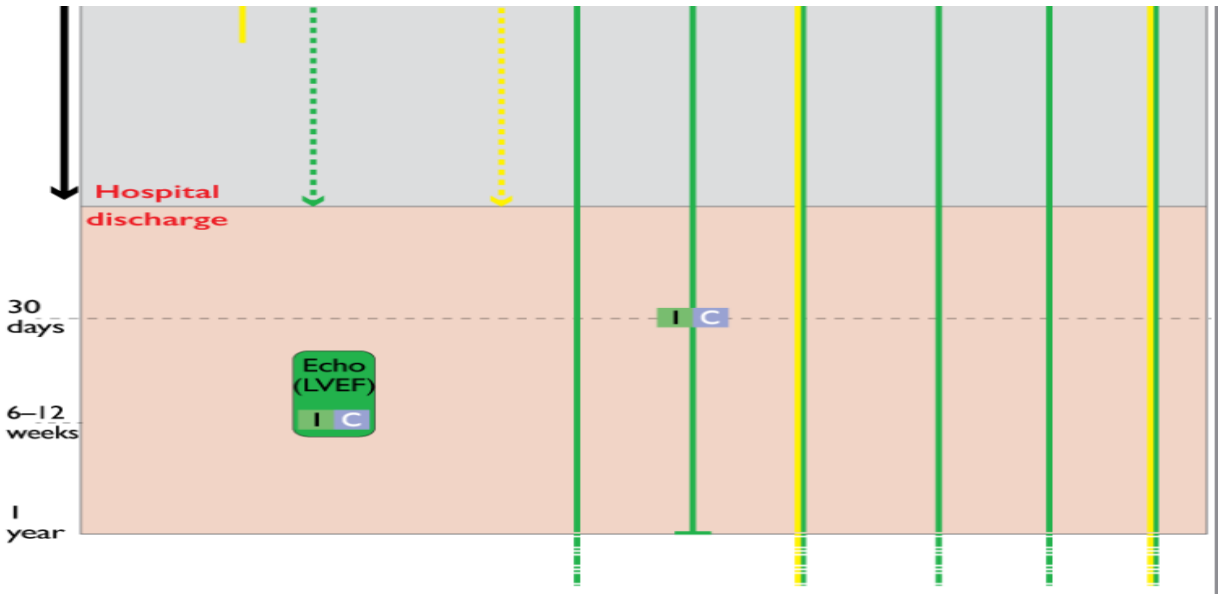


Figure 6 "Do not forget" interventions in STEMI patients undergoing a successful fibrinolysis





Mostly prescribed interventions (Class I, green, and IIa, light yellow) are presented along with the expected timing of delivery. Solid lines represent recurrent (daily) intervention. Double-arrowed dashed lines represent a time-window in which the intervention can be delivered.

[1]Enoxaparin dose: 30 mg *i.v.* bolus followed by 1 mg/kg subcutaneous every 12 hours (dose adjustment for ≥75 years and renal insufficiency is presented in Table 9).Unfractionated heparin is an alternative to enoxaparin.

[2]Aspirin loading dose: 150–300 mg chewed or 75–250 mg intravenous.

[3]Clopidogrel loading dose: 300 mg oral (75 mg in ≥75 years).

[4]Aspirin maintenance dose: 75–100 mg oral.

[5]Clopidogrel maintenance therapy: 75 mg daily.

[6]48 hours after fibrinolysis, switch to prasugrel/ticagrelor may be considered in PCI-treated patients.

Recommendations for the management of left ventricular dysfunction and acute heart failure in ST-elevation myocardial infarction

Recommendations	Class[a]	Level[b]
ACE-inhibitor (or if not tolerated,ARB) therapy is indicated as soon as haemodynamically stable for all patients with evidence of LVEF ≤40% and/or heart failure to reduce the risk of hospitalization and death.	I	A
Beta-blocker therapy is recommended in patients with LVEF ≤40% and/or heart failure after stabilization, to reduce the risk of death, recurrent MI, and hospitalization for heart failure.	I	A
An MRA is recommended in patients with heart failure and LVEF ≤40% with no severe renal failure or hyperkalaemia to reduce the risk of cardiovascular hospitalization and death.	I	B
Loop diuretics are recommended in patients with acute heart failure with symptoms/signs of fluid overload to improve symptoms.	I	C
Nitrates are recommended in patients with symptomatic heart failure with SBP >90 mmHg to improve symptoms and reduce congestion.	I	C
Oxygen is indicated in patients with pulmonary oedema with SaO_2 <90% to maintain a saturation >95%.	I	C
Patient intubation is indicated in patients with respiratory failure or exhaustion, leading to hypoxaemia, hypercapnia, or acidosis, and if non- invasive ventilation is not tolerated.	I	C
Non-invasive positive pressure ventilation (continuous positive airway pressure, biphasic positive airway pressure) should be considered in patients with respiratory distress (respiratory rate >25 breaths/min, SaO_2 <90%) without hypotension.	IIa	B
Intravenous nitrates or sodium nitroprusside should be considered in patients with heart failure and elevated SBP to control blood pressure and improve symptoms.	IIa	C
Opiates may be considered to relieve dyspnoea and anxiety in patients with pulmonary oedema and severe dyspnoea. Respiration should be monitored.	IIb	B
Inotropic agents may be considered in patients with severe heart failure with hypotension refractory to standard medical treatment.	IIb	C

Recommendations for the management of cardiogenic shock in ST-elevation myocardial infarction

Recommendations	Class[a]	Level[b]
Immediate PCI is indicated for patients with cardiogenic shock if coronary anatomy is suitable. If coronary anatomy is not suitable for PCI, or PCI has failed, emergency CABG is recommended.	I	B
Invasive blood pressure monitoring with an arterial line is recommended.	I	C
Immediate Doppler echocardiography is indicated to assess ventricular and valvular functions, loading conditions, and to detect mechanical complications.	I	C
It is indicated that mechanical complications are treated as early as possible after discussion by the Heart Team.	I	C
Oxygen/mechanical respiratory support is indicated according to blood gases.	I	C
Fibrinolysis should be considered in patients presenting with cardiogenic shock if a primary PCI strategy is not available within 120 min from STEMI diagnosis and mechanical complications have been ruled out.	IIa	C
Complete revascularization during the index procedure should be considered in patients presenting with cardiogenic shock.	IIa	C
Intra-aortic balloon pumping should be considered in patients with haemodynamic instability/cardiogenic shock due to mechanical complications.	IIa	C
Haemodynamic assessment with pulmonary artery catheter may be considered for confirming diagnosis or guiding therapy.	IIb	B
Ultrafiltration may be considered for patients with refractory congestion, who failed to respond to diuretic-based strategies.	IIb	B
Inotropic/vasopressor agents may be considered for haemodynamic stabilization.	IIb	C
Short-term mechanical support[c] may be considered in patients in refractory shock.	IIb	C
Routine intra-aortic balloon pumping is not indicated.	III	B

CABG = coronary artery bypass graft surgery; ECLS = extracorporeal life support; ECMO = extracorporeal membrane oxygenation; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

[a]Class of recommendation - [b]Level of evidence - [c]Percutaneous cardiac support devices, ECLS, and ECMO.

Management of atrial fibrillation		
Recommendations	**Class[a]**	**Level[b]**
Acute rate control of AF		
Intravenous beta-blockers are indicated for rate control if necessary and there are no clinical signs of acute heart failure or hypotension.	I	C
Intravenous amiodarone is indicated for rate control if necessary in the presence of concomitant acute heart failure and no hypotension.	I	C
Intravenous digitalis should be considered for rate control if necessary in the presence of concomitant acute heart failure and hypotension.	IIa	B
Cardioversion		
Immediate electrical cardioversion is indicated when adequate rate control cannot be achieved promptly with pharmacological agents in patients with AF and ongoing ischaemia, severe haemodynamic compromise or heart failure.	I	C
Intravenous amiodarone should be considered to promote electrical cardioversion and/or decrease risk for early recurrence of AF after electrical cardioversion in unstable patients with recent onset AF.	I	C
In patients with documented de novo AF during the acute phase of STEMI, long-term oral anticoagulation should be considered depending on CHA_2DS_2-VASc score and taking concomitant antithrombotic therapy into account.	IIa	C
Digoxin is ineffective in converting recent onset AF to sinus rhythm and is not indicated for rhythm control.	III	A
Calcium channel blockers and beta-blockers including sotalol are ineffective in converting recent onset AF to sinus rhythm.	III	B
Prophylactic treatment with antiarrhythmic drugs to prevent AF is not indicated.	III	B

AF = atrial fibrillation; CHA2DS2-VASc = Cardiac failure, Hypertension, Age ≥75 (Doubled), Diabetes, Stroke (Doubled) – VAScular disease, Age 65–74 and Sex category (Female); STEMI = ST-segment elevation myocardial infarction. [a]Class of recommendation - [b]Level of evidence.

Management of ventricular arrhythmias and conduction disturbances in the acute phase		
Recommendations	**Class[a]**	**Level[b]**
Intravenous beta-blocker treatment is indicated for patients with polymorphic VT and/or VF unless contra-indicated.	I	B
Prompt and complete revascularization is recommended to treat myocardial ischaemia that may be present in patients with recurrent VT and/or VF.	I	C
Intravenous amiodarone is recommended for treatment of recurrent polymorphic VT.	I	C
Correction of electrolyte imbalances (especially hypokalaemia and hypomagnesemia) is recommended in patients with VT and/or VF.	I	C
In cases of sinus bradycardia with haemodynamic intolerance or high degree AV block without stable escape rhythm:		
• *i.v.* positive chronotropic medication (epinephrine, vasopressin and/or atropine) is indicated	I	C
• temporary pacing is indicated in cases of failure to respond to positive chronotropic medication	I	C
• urgent angiography with a view to revascularization is indicated if the patient has not received previous reperfusion therapy.	I	C
Intravenous amiodarone should be considered for recurrent VT with haemodynamic intolerance despite repetitive electrical cardioversion.	IIa	C
Transvenous catheter pace termination and/or overdrive pacing should be considered if VT cannot be controlled by repetitive electrical cardioversion.	IIa	C
Radiofrequency catheter ablation at a specialized ablation centre followed by ICD implantation should be considered in patients with recurrent VT, VF, or electrical storm despite complete revascularization and optimal medical therapy.	IIa	C
Recurrent VT with haemodynamic repercussion despite repetitive electrical cardioversion may be treated with lidocaine if beta-blockers, amiodarone, and overdrive stimulation are not effective/applicable.	IIb	C
Prophylactic treatment with antiarrhythmic drugs is not indicated and may be harmful.	III	B
Asymptomatic and haemodynamically irrelevant ventricular arrhythmias should not be treated with antiarrhythmic drugs.	III	C

Long-term management of ventricular arrhythmias and risk evaluation for sudden death		
Recommendations	**Class[a]**	**Level[b]**
ICD therapy is recommended to reduce sudden cardiac death in patients with symptomatic heart failure (NYHA Class II–III) and LVEF ≤35% despite optimal medical therapy for >3 months and ≥6 weeks after MI, who are expected to survive for at least 1 year with good functional status.	I	A
ICD implantation or temporary use of a wearable cardioverter defibrillator may be considered <40 days after MI in selected patients (incomplete revascularization, pre-existing LVEF dysfunction, occurrence of arrhythmias >48 hours after STEMI onset, polymorphic VT or VF).	IIb	C

MINOCA

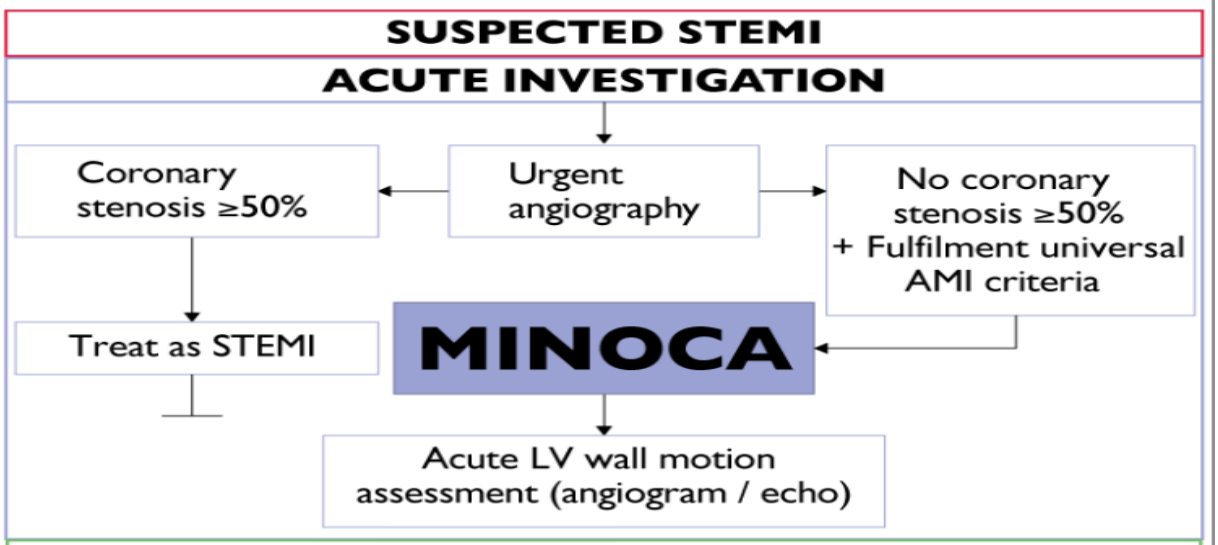
In 1–14% of MI patients there is absence of obstructive CAD. The demonstration of non-obstructive CAD in a patient presenting with symptoms suggestive of ischaemia and ST-segment elevation or equivalent does not preclude an atherothrombosis aetiology. MINOCA is a working diagnosis and should lead the treating physician to investigate underlying causes.

The identification of the underlying cause of MINOCA should lead to specific treatment strategies. Although the outcome of MINOCA strongly depends on the underlying cause, its overall prognosis is serious, with a 1-year mortality of about 3.5%.

Table 10 Diagnostic criteria for myocardial infarction with non- obstructive coronary arteries
The diagnosis of MINOCA is made immediately upon coronary angiography in a patient presenting with features consistent with an AMI, as detailed by the following criteria:
(1) Universal AMI criteria.
(2)Non-obstructive coronary arteries on angiography, defined as no coronary artery stenosis ≥50% in any potential IRA.
(3) No clinically overt specific cause for the acute presentation.

AMI = acute myocardial infarction; IRA = infarct-related artery;
MINOCA = myocardial infarction with non-obstructive coronary arteries.

Figure 7 Diagnostic test flowchart in MINOCA



SUSPECTED DIAGNOSIS AND FURTHER DIAGNOSTIC TESTS

	Non-invasive	Invasive
Myocarditis	**TTE Echo** (pericardial effusion) **CMR** (myocarditis[2], pericarditis)	**Endomyocardial biopsy** (myocarditis)
Coronary (epicardial/ microvascular)	**TTE Echo** (Regional wall motion abnormal-ities, embolic source) **CMR** (small infarction) **TOE/Bubble Contrast Echo** (Patent foramen ovale, atrial septal defect	**IVUS/OCT** (plaque disruption /dissection) **Ergonovine/ Ach test**[1] (spasm) **Pressure/ Doppler wire** (microvascular dysfunction)
Myocardial disease	**TTE Echo** **CMR** (Takotsubo, others)	
Pulmonary Embolism	**D-dimer** (Pulmonary embolism) **CT scan** (Pulmonary embolism) **Thrombophilia screen**	
Oxygen supply/ demand imbalance- Type 2 MI	**Blood tests, Extracardiac investigation**	

CMR = Cardiac Magnetic Resonance; IVUS = IntraVascular UltraSound; LV = Left Ventricle; MINOCA = Myocardial Infarction with Non-Obstructed Coronary Arteries; OCT = Optical Coherence Tomography; STEMI = ST segment Elevation Myocardial Infarction; TOE = Trans-Oesofageal Echocardiography; TTE = Trans-Thoracic Echocardiography.

Takotsubo syndrome cannot be diagnosed with certainty in the acute phase as the definition requires follow up imaging to document recovery of left ventricular function. IVUS and OCT frequently show more atherosclerotic plaque than may be appreciated on angiography.They also increase sensitivity for dissection. If intracoronary imaging is to be performed, it is appropriate to carry out this imaging at the time of the acute cardiac catheterization, after diagnostic angiography. Patients should be made aware of the additional information the test can provide and the small increase in risk associated with intracoronary imaging.

[1]Provocative testing for coronary artery spasm might be considered in selected patients with a recent AMI with suspected vasospastic angina. Provocative manoeuvres have to be always performed by operators with experience and not necessarily in the acute phase of STEMI.

[2]Clinically suspected myocarditis by ESC Task Force criteria = No angiographic stenosis ≥50% plus non ischemic pattern on CMR. Definite myocarditis by ESC Task Force criteria = No angiographic stenosis ≥50% plus endomyocardial biopsy confirmation (histology, immunohistology, polymerase-chain reaction based techniques to search for genome of infectious agents, mainly viruses).

It is recommended that STEMI networks and their individual components establish measurable quality indicators, systems to measure and compare these indicators, perform routine audits and implement strategies to ensure that every patient with STEMI receives the best possible care according to accepted standards and has the best possible outcomes. Quality indicators are intended to measure and compare the quality of health-service provision and serve as a foundation for quality improvement initiatives.

Table 11 Quality indicators

Type of indicator and process	Quality indicator
Structural measures (organization)	1) The centre should be part of a network specifically developed for the rapid and efficient management of STEMI patients with written protocols covering the following points: • *Single emergency telephone number* for patients to contact the emergency services • *Pre-hospital interpretation of the ECG* for diagnosis and strategy decision • *Pre-hospital activation* of the catheterization laboratory • *Transportation* (ambulance-helicopter) equipped with ECG defibrillators. 2) Key times to reperfusion are systematically recorded and periodically reviewed for quality assessments by the centre or network participants.

Performance measures for reperfusion therapy	1) Proportion of STEMI patients arriving in the first 12 h receiving reperfusion therapy. 2) Proportion of patients with timely reperfusion therapy, defined as: • For patients attended to in the pre-hospital setting: – <90 min from STEMI diagnosis to IRA wire crossing for reperfusion with PCI – <10 min from STEMI diagnosis to lytic bolus for reperfusion with fibrinolysis • For patients admitted to PCI centres: – <60 min from STEMI diagnosis to IRA wire crossing for reperfusion with PCI • For transferred patients: – <120 min from STEMI diagnosis to IRA wire crossing for reperfusion with PCI – <30 min door-in-door-out for patients presenting in a non- PCI centre (en route to a PCI centre)
Performance measures for risk assessment in hospital	1) Proportion of patients having LVEF assessed before discharge.
Performance measures for antithrombotic treatment in hospital	1) Proportion of patients without a clear and documented contra-indication for aspirin and/or a $P2Y_{12}$ inhibitor, discharged on DAPT.
Performance measures for discharge medication and counselling	1) Proportion of patients without contra-indications with a statin (high-intensity) prescribed at discharge. 2) Proportion of patients with LVEF ≤40% or clinical evidence of heart failure and without contra-indications with a beta-blocker prescribed at discharge. 3) Proportion of patients with LVEF ≤40% or clinical evidence of heart failure without contra-indications with an ACE-inhibitor (or ARB if not tolerated) prescribed at discharge. 4) Proportion of patients with smoking cessation advice/counselling at discharge. 5) Proportion of patients without contra-indications enrolled in a secondary prevention/cardiac rehabilitation programme at discharge.
Patient-reported outcomes	• Availability of a programme to obtain feedback regarding the patient's experience and quality of information received, including the following points: – Angina control. – Explanations provided by doctors and nurses (about the disease, benefit/risk of discharge treatments, and medical follow-up). – Discharge information regarding what to do in case of recurrence of symptoms and recommendation to attend a rehabilitation programme (including smoking cession and diet counselling).
Outcome measures	1) 30-day adjusted mortality (e.g. GRACE risk score-adjusted). 2) 30-day adjusted readmission rates.
Opportunity-based composite quality indicators	• Proportion of patients with LVEF >40% and no evidence of heart failure receiving at discharge low-dose aspirin and a $P2Y_{12}$ inhibitor and high-intensity statins. • Proportion of patients with LVEF ≤40% and/or heart failure receiving at discharge low-dose aspirin, a $P2Y_{12}$ inhibitor, high-intensity statins, an ACE-inhibitor (or ARB), and a beta-blocker